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MAIL STOP APPEAL BRIEF-PATENTS
Attorney Docket No. 24948

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:

	POPP	Conf No.:	3528
Serial No:	10/617,191	Examiner:	Channavajjala, Lakshmi Sarada
Filed:	July 11, 2003	Art Unit:	1611

For: **TOPICAL FORMULATIONS FOR TREATMENT OF SKIN DISORDERS**

TRANSMITTAL LETTER

Commissioner for Patents
Box 1450
Alexandria, VA 22313-1450

Sir:

Submitted herewith for filing in the U.S. Patent and Trademark Office is the following:

(1) Transmittal Letter;
(2) Appeal Brief;
(3) Appendix A (Claims on Appeal); and
(4) Check No. 6420 in the amount of $510.00 for the fee required for filing a brief in support of appeal.

The Commissioner is hereby authorized to charge any deficiency or credit any excess to Deposit Account Number 14-0112.

Respectfully submitted,
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Date: August 21, 2008

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APPEAL BRIEF

This is an appeal to the Board of Patent Appeals and Interferences from the decision of Examiner Channavajjala, Lakshmi Sarada, mailed February 4, 2008, rejecting claims 26-31. Since these claims have been twice rejected for the same reason, appellants filed a Notice of Appeal on July 1, 2008 under MPEP §1204. This Appeal Brief is due two months from the time the Notice of Appeal is filed. Therefore this Appeal Brief is timely filed.

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REAL PARTY IN INTEREST

The real party in interest is the assignee, STIEFEL LABORATORIES, INC.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

STATUS OF CLAIMS

Claims 1-25 and 32-37 have been cancelled. Claims 26-31 are pending. Claims 26-31 have been rejected, the rejection thereof is hereby appealed. The claims appealed are reproduced in the Appendix appearing in this paper on page 29.

STATUS OF AMENDMENTS

No claim amendments have been entered since the Official Action dated February 4, 2008 was mailed.

SUMMARY OF CLAIMED SUBJECT MATTER

The presently claimed subject matter relates to a process for preparing a storage-stable topical composition for treating a skin disorder or condition. The presently claimed process requires mixing a benzoyl peroxide intermediate dispersion having a viscosity of 60,000 to 250,000 centipoises (cp) and a clindamycin intermediate solution, such that the final composition has a viscosity of 50,000 to 200,000 cp which is lower than the viscosity of the benzoyl peroxide dispersion before mixing.

In particular, the only independent claim 26 on appeal is directed to a process for preparing a storage-stable topical composition for treating a skin disorder or condition, which comprises the steps of: (a) forming at a temperature of about 15 to about 25^{o}C a benzoyl peroxide intermediate dispersion having a viscosity of about 60,000 to about 250,000 cp sufficient to yield a composition which contains between about 2.25% and about 12.5% by weight benzoyl peroxide in the final product; (b) forming at a temperature of about 15 to about 25^{o}C a clindamycin intermediate solution sufficient to yield a composition which contains between about 0.5% and about 1.5% by weight clindamycin active in the final product; and (c) mixing said benzoyl peroxide intermediate dispersion and said clindamycin intermediate solution under conditions sufficient to yield a benzoyl peroxide and clindamycin mixture having a final pH of between about 4.5 to about 5.0, wherein said mixture has a viscosity lower than the viscosity of the benzoyl peroxide intermediate dispersion, wherein the viscosity of the mixture is of about 50,000 to about 200,000 cp, and wherein said composition comprises sufficient inactive ingredients to provide storage stability and effectiveness for a treatment period.

Support for claim 26 may be found throughout the specification and claims as originally filed, for example, at page 8, line 23 through page 9, line 19; page 12, lines

12-16; page 15, lines 2-9; and page 27, line 2 through page 28, line 5.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 26-31 are unpatentable under 35 U.S.C. §103(a) over Baroody et al. in U.S. Patent No. 6,117,843.

ARGUMENTS

I: Claims 26-31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Baroody et al. in U.S. Patent No. 6,117,843

Claims 26-31 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Baroody et al. in U.S. Patent No. 6,117,843 for the reasons set forth in the Office Action dated February 4, 2008.

As the basis of this rejection, the Examiner states in relevant part that:

> With respect to the viscosity, Baroody discloses that initial viscosity of benzoyl peroxide is in the range of 50,000 to 90,000 and a final viscosity in the range of 70,000 to 120,000. Instant claims require that the viscosity of the mixture of benzoyl peroxide and clindamycin is lower than the viscosity of benzoyl peroxide dispersion. Baroody does not teach the purity of benzoyl peroxide, viscosity of benzoyl peroxide, the percentage degradation of clindamycin or the amount of benzoyl peroxide and clindamycin in the claimed standard deviation. However, the instant claims do not state what the initial and final viscosities are and in addition, recites initial and final viscosities that overlap with each other, thus allowing for very little difference between the initial and final viscosities.
>
> Baroody also recognizes the same factors i.e., pH, viscosity etc. that affect that stability (result-affective variables) of the composition and therefore it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to employ pure active compounds and optimize the general conditions such as viscosity, amounts of active agents with an expectation to achieve a composition that stable for long periods of time because the teachings of Baroody are also directed to preparing a storage stable composition comprising benzoyl peroxide and clindamycin and employed for the same purpose similar to the instant invention i.e., treatment of acne or other skin related conditions that need require benzoyl peroxide and clindamycin combination. In this regard applicants have not shown the criticality of the initial and final viscosities as a function of stability of the composition. See, pages 3 and 4 of the Official Action
>
> In response, a person of ordinary skill in the art reading Baroody would readily recognize that maintaining stability of the composition is important and in order to do so, factors such as pH, viscosity, amounts of gelling agent etc., should be varied. Baroody recognizes the above factors as result effective variables and hence the application of the technique to

> stabilize the composition is not beyond the skill of an ordinary person, which according to the above KSR ruling would have been obvious. The reasonable expectation in this case is that varying the pH and gelling agents and viscosity results in variable stability of the composition. See, id. at page 7.

Appellants respectfully traverse this rejection. To establish a *prima facie* case of obviousness, the Examiner must satisfy three requirements. First, as the U.S. Supreme Court very recently held in KSR International Co. v. Teleflex Inc. et al., Slip Opinion No. 04–1350, 550 U. S. ____ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (KSR, *supra*, slip opinion at 13-15.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Amgen Inc. v. Chugai Pharm. Co., 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

A *prima facie* case of obviousness must also include a showing of the reasons

why it would be obvious to modify the references to produce the present claims. Ex parte Clapp, 277 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). The Examiner bears the initial burden to provide some convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings. Id. at 974.

Further, appellants note that a *prima facie* case of obviousness can be rebutted if applicants can show "that the art in any material respect taught away" from the claimed invention, In re Geisler, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997), or the claimed invention yields unexpectedly improved properties or properties not presented in the prior art. In re Dillon, 919 F.2d at 692-93, 16 USPQ2d at 1901.

Appellants respectfully traverse this rejection because all of the three requirements for a *prima facie* case of obviousness have not been established for the rejection of these claims. In particular, the Examiner failed to establish a *prima facie* case of obviousness because one of ordinary skill in the art would have had no suggestion or motivation to modify the elements shown by the cited reference to arrive at the presently pending claims. Further, any potential *prima facie* case of obviousness is rebutted in the present application because the teachings contained in the prior art teach away from the presently claimed process. In addition, the presently claimed process provides improved properties or properties not present in the prior art.

A. The presently claimed subject matter

Independent claim 26 is directed to a process for preparing a storage-stable topical composition for treating a skin disorder or condition, which comprises the steps of:

(a) forming at a temperature of about 15 to about 25^{o}C a benzoyl peroxide

intermediate dispersion having a viscosity of about 60,000 to about 250,000 centipoises sufficient to yield a composition which contains between about 2.25% and about 12.5% by weight benzoyl peroxide in the final product;

(b) forming at a temperature of about 15 to about 25 ^{o}C a clindamycin intermediate solution sufficient to yield a composition which contains between about 0.5% and about 1.5% by weight clindamycin active in the final product; and

(c) mixing said benzoyl peroxide intermediate dispersion and said clindamycin intermediate solution under conditions sufficient to yield a benzoyl peroxide and clindamycin mixture having final pH of between about 4.5 to about 5.0,

wherein said mixture has a viscosity lower than the viscosity of the benzoyl peroxide intermediate dispersion,

wherein the viscosity of the mixture is of about 50,000 to about 200,000 centipoises, and

wherein said composition comprises sufficient inactive ingredients to provide storage stability and effectiveness for a treatment period.

Claims 27-31 depend either directly or indirectly from claim 26. If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

B. The Prior Art

Baroody et al., a single reference, teaches a process for the preparation of a topical composition by combining two separately maintained components by simple mixing prior to use. See, Baroody et al. col. 3, lines 14-28. The two components are an aqueous gel suspension of benzoyl peroxide and an aqueous solution of a clindamycin

salt or ester, preferably further combined with an aqueous gelling agent. See, id. at col. 4, lines 27-32. The gelling agent is initially combined with an aqueous suspension of benzoyl peroxide to form a first component of a two component kit for formulating the topical composition, and the gelling agent ideally is selected to have a reduced viscosity at the pH of the first component and an increased viscosity at the stage of the final product. See, id. at col. 4, lines 44-52.

Regarding the viscosities of the benzoyl peroxide suspension and the final product, Baroody et al. further teaches that the lower viscosity of the benzoyl peroxide component makes the combination and mixing with the clindamycin component easier, while the final topical composition can still possess the desired higher viscosity, gel consistency. See, id. at col. 5, lines 48-52. Preferably, the viscosity of the benzoyl peroxide component will be below about $9x10^4$ cp, usually being in the range from $5x10^4$ cp to $9x10^4$ cp, more preferably being in the range from $6.5x10^4$ cp to $8.5x10^4$ cp, while the viscosity of the final topical composition product will be in the range from $7x10^4$ cp to $12x10^4$ cp, more preferably being in the range from $8x10^4$ cp to $10x10^4$ cp. See, id. at col. 5, lines 58-64. When the benzoyl peroxide component is combined with the clindamycin component, the resulting combined product will have an increased pH resulting in enhanced viscosity within the range set forth above. See, id. at col. 6, lines 3-6. Further, Baroody et al. teaches that the increased viscosity in the final product is beneficial. See, id. at col. 6, lines 23-26.

C. No Suggestion or Motivation to Modify the Process in Baroody et al. to Reach the Presently Claimed Process

Appellants respectfully assert that one of ordinary skill in the art would have had no suggestion or motivation to modify the process taught in the Baroody et al. reference to reach the presently claimed process at the time the present invention was made.

Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so. In re Kahn, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006). If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). If the proposed modification or combination of the prior art would change the principle of operation of the prior art being modified, the teachings of the references are not sufficient to render the claims *prima facie* obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

In In re Gordon, the claimed device was a blood filter assembly for use during medical procedures wherein both the inlet and outlet for the blood were located at the bottom end of the filter assembly, and wherein a gas vent was present at the top of the filter assembly. The cited prior art reference taught a liquid strainer for removing dirt and water from gasoline and other light oils wherein the inlet and outlet were at the top of the device, and wherein a pet-cock (stopcock) was located at the bottom of the device for periodically removing the collected dirt and water. The reference further taught that the separation is assisted by gravity. The Board of Patent Appeals and Interferences (the Board) concluded the claims were *prima facie* obvious, reasoning that it would have

been obvious to turn the reference device upside down. However, the Court of Appeals for the Federal Circuit (CAFC) reversed the decision by the Board, finding that if the prior art device was turned upside down it would be inoperable for its intended purpose because the gasoline to be filtered would be trapped at the top, the water and heavier oils sought to be separated would flow out of the outlet instead of the purified gasoline, and the screen would become clogged.

In the present application, as discussed above, the Baroody et al. reference, as a whole, teaches a process for the preparation of a storage stable topical composition by the simple mixing of an aqueous gel suspension of benzoyl peroxide and an aqueous solution of a clindamycin salt or ester, where a gelling agent is initially combined with the benzoyl peroxide suspension and is selected to have a reduced viscosity at the pH of the benzoyl peroxide suspension and an increased viscosity at the stage of the final product, to make the mixing easier. Accordingly, the process in the Baroody et al. reference, if modified in the opposite way with regard to the viscosities of the benzoyl peroxide suspension and the final composition, would be unsatisfactory because the modification would make the mixing harder under the conditions and parameters suggested by the Baroody et al. reference. Accordingly, there is no suggestion or motivation to modify the process in the Baroody et al. reference to arrive at the present claims, as required by In re Gordon.

Furthermore, this unsatisfactory modification would also change the principle of operation of the Baroody et al. process and composition. In this regard, appellants note that the Baroody et al. reference would predict the inability to prepare a storage stable topical composition due to the difficulty in mixing the various components, resulting from the change of the viscosities in the opposite direction to that shown by Baroody et al.

According to the Baroody et al. disclosure, the process requirements necessary to prepare a final composition with a viscosity lower than that of the benzoyl peroxide intermediate dispersion, as presently claimed, would negatively affect the homogeneity and gel consistency in the final composition, and ultimately, the storage stability of the final composition. Accordingly, the Baroody et al. reference, on its face, provides no suggestion or motivation to modify the disclosed process to arrive at the present claims , as required by In re Ratti.

As such, there is no suggestion or motivation to modify the Baroody et al. process to reach the presently claimed process, and in this respect, the Examiner has failed to establish a *prima facie* case of obviousness.

D. Baroody et al. Teaches Away from the Presently Claimed Process

Additionally, the disclosure contained in the Baroody et al. reference in substance teaches away from the presently claimed process.

A *prima facie* case of obviousness can be rebutted if applicant can show "that the art in any material respect taught away" from the claimed invention. In re Geisler, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the application. In re Gurley, 31 USPQ2d 1130 (Fed. Cir. 1994). A reference teaches away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant. United States v. Adams, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966).

Further, portions of a reference arguing against or teaching away from the claimed invention must be considered. See Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc., 230 USPQ 416 (Fed. Cir. 1986). Thus, the rule of law clearly requires that the Examiner consider a reference in its entirety in determining the scope and content of the reference. W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, (Fed. Cir 1983), *cert. denied*, 469 U.S. 851 (1984). The Examiner therefore must acknowledge any disclosure in the reference that teaches away from the presently pending claims. Id.

Further, the totality of the prior art must be considered and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. In re Hedges, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986).

i. Teaching-Away Portions in Baroody et al.

As previously noted, the Baroody et al. reference teaches away from the presently claimed process. Throughout the specification, in particular in the Description of Preferred Embodiments, the Baroody et al. reference expressly and repeatedly teaches the selection of a gelling agent in such a way that the initial viscosity of the benzoyl peroxide suspension is relatively lower while the viscosity of the final product is relatively higher. Furthermore, as a benefit of this selection, the Baroody et al. reference teaches that the mixing will be easier and the final topical composition can still possess the desired higher viscosity, gel consistency:

> [A]dditionally, by properly selecting the gelling agent, the initial viscosity of the benzoyl peroxide suspension (at the suspension pH) may be relatively low, while the viscosity of the final product (at the product pH), can be relatively high to provide a desired gel consistency. Thus, the components

may be easily combined by a pharmacist to provide a gel having a pleasing consistency and texture for use by the patient. See, Baroody et al. col. 3, lines 29-36.

[T]he gelling agent ideally will be selected to have a reduced viscosity at the pH of the first component and an increased viscosity at the stage of the final product obtained when the two components are combined. See, id. at col. 4, lines 48-52.

[B]y properly selecting the nature of the gelling agent and the pH of the benzoyl peroxide component, the benzoyl peroxide component itself may be maintained at a relatively low viscosity while the final topical composition (which is at a different pH) will have a relatively higher viscosity. In this way, mixing of the two components to form the topical composition is facilitated (i.e. the lower viscosity of the benzoyl peroxide component makes the combination and mixing with the clindamycin component easier) while the final topical composition can still possess the desired higher viscosity, gel consistency. See, id. at col. 5, lines 46-57.

[P]referably, the viscosity of the benzoyl peroxide component will be below about $9x10^4$, usually being in the range from $5x10^4$ cp to $9x10^4$, more preferably being in the range from $6.5x10^4$ cp to $8.5x10^4$ cp, while the viscosity of the final topical composition product will be in the range from $7x10^4$ cp to $12x10^4$ cp, more preferably being in the range from $8x10^4$ cp to $10x10^4$ cp. These viscosities may be achieved using the polymeric gelling agents, as described above, and a benzoyl peroxide component having a pH in the range from 3.5 to 7.0, preferably in the range from 4.0 to 5.0. The pH may be adjusted by the addition of a pharmaceutically acceptable buffer or base, such as potassium hydroxide. When the benzoyl peroxide component is combined with the clindamycin component, the resulting combined product will have an increased pH resulting in enhanced viscosity within the range set forth above. See, id. at col. 5, line 58 through col. 6, line 6.

[T]hus, it can be seen that a beneficial increase in viscosity can be achieved by increasing the pH of the final (combined) product relative to the initial pH of the benzoyl peroxide component containing the gelling

agent. See, id. at col. 6, lines 22-25.

As such, the Baroody et al. reference expressly and repeatedly teaches that when preparing a storage stable topical composition comprising benzoyl peroxide and clindamycin, it is beneficial to have a relatively lower viscosity for the benzoyl peroxide suspension and a relatively higher viscosity for the final topical composition, to facilitate the mixing of the two components and the formation of a final stable composition.

In contrast, in the presently claimed process, it is necessarily required that the viscosity of the benzoyl peroxide intermediate dispersion is relatively higher than the viscosity of the final mixture. In particular, the claimed process requires that the benzoyl peroxide intermediate dispersion, prior to mixing, has a preferred viscosity of about 60,000 cp to about 250,000 cp, the final composition, after mixing, has a preferred viscosity of about 50,000 cp to 200,000 cp, and at the same time, the viscosity of the benzoyl peroxide intermediate dispersion is relatively higher than the viscosity of the final composition.

Accordingly, the teachings in the Baroody et al. reference would have discouraged a person of ordinary skill in the art from following, practicing, or even attempting the presently claimed process to prepare a storage stable topical composition containing benzoyl peroxide and clindamycin. In other words, a person of ordinary skill in the art would have been led in a direction divergent from the path that was taken by the present application.

ii. Examiner's Failure to Consider the Teaching-Away Portion in Baroody et al.

The Examiner has failed to consider the Baroody et al. reference in its entirety,

particularly the teaching-away portion noted above. The teachings of the Baroody et al. reference, as mentioned above, do not represent a mere disclosure of more than one alternative, as described by In re Fulton, 391 F. 3d 1195, 1201, 73 USPQ2d 1141, 1146, nor such insubstantial description, as described by In re Gurley. Therefore, the portions of Baroody et al. that teach away from the present claims should have been considered by the Examiner as a significant factor in determining the obviousness of the present claims. However, the Examiner has ignored these teaching-away portions in the Baroody et al. reference. Nowhere in the Final Official Action dated August 13, 2007 and the subsequent Non-final Official Action dated February 4, 2008 did the Examiner consider the teaching-away portions in the Baroody et al. reference as a significant factor in determining the obviousness of the present claims. Without providing any comments on the teaching-away portions of the reference or on the reasons why it is obvious for a person of ordinary skill in the art to modify the process in the Baroody et al. reference in spite of the teaching-away portions, the Examiner maintained her opinion: Since Baroody et al. recognizes and suggests that several factors such as pH, viscosity and a gelling agent contributed to the stability, these are result effective variables, and the modification of any such variables to stabilize the composition is not beyond the skill of an ordinary person. See, at page 6 line 18 through page 7 line 1; page 7 lines 15-20 of the Official Action dated Feb. 4, 2008.

The Baroody et al. reference, however, contrary to the Examiner's indication, does not teach the viscosity as a result-effective variable only for the stability of the topical composition. Rather, Baroody et al. further expressly teaches how to set both the viscosities in the benzoyl peroxide suspension and in the final composition, in order to obtain the beneficial effect of facilitating the mixing of the two components and achieving

a gel consistency. Specifically, Baroody et al. discloses that the viscosity of the benzoyl peroxide suspension is preferably relatively lower while the viscosity of the final composition is preferably relatively higher. This is achieved by properly selecting a gelling agent or by increasing the pH of the final composition relative to the initial pH of the benzoyl peroxide intermediate dispersion containing the gelling agent.

The Examiner has never considered the teaching-away portions of the Baroody et al. reference disclosure as a significant factor in the obviousness rejections of claims 26-31. Accordingly, appellants respectfully assert that the Examiner has failed to consider the Baroody et al. reference in its entirety, including the teaching-away portions, as required by the rule of law.

iii. Contrary to the Accepted Wisdom: In re Hedges

Appellants respectfully further assert that the scope of the present claims is contrary to the accepted knowledge in the art as disclosed in the Broody et al. reference, and that this should be considered as further evidence of nonobvious.

The totality of the prior art must be considered and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. In re Hedges, 783 F.2d 1038 (Fed. Cir. 1986) The Hedges court reversed the decision by the Board rejecting the Hedges process claims 8-10 (Serial No. 301,396) as being unpatentable over the Felix patent (US Patent No. 2,010,754), holding that Hedges proceeded contrary to the accepted wisdom and this is strong evidence of unobviouness. Id.

In particular, in In re Hedges, the claimed invention was the reaction of diphenyl sulfone, at a temperature above its melting point of 127°C, with liquid or gaseous sulfur trioxide in the absence of water or a solvent, thereby sulfonating the sulfone in high

yields without forming the sulfuric acid by-product. The only pending rejection was made under 35 U.S.C. §103(a) and relied only on the Felix patent. The Felix patent showed the sulfonation of aryl sulfones with sulfur trioxide in the form of fuming sulphuric acid. Sulfonation was carried out at 5-10°C, after which the temperature rose exothermically to 30°C before it was lowered to room temperature. The Board held that this disclosure, without more, presented a *prima facie* case of obviousness. However, the CAFC did not agree with the Board that Felix alone supported a *prima facie* case of obviousness and found that Felix makes clear that low temperatures are the desired conditions for this reaction. According to the CAFC, only after the USPTO has made a *prima facie* case of obviousness does the burden of coming forward shift to the applicant. In re Rinehart, 531 F.2d 1048, 1051, 189 USPQ 143, 147 (CCPA 1976). If a prima facie case is made in the first instance, and if applicant comes forward with a reasonable rebuttal, whether buttressed by experiment, prior art reference, or argument, the entire merits of the matter are to be reweighed. In re Piasecki, 745 F.20 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984).

Further, in response to the Board argument that Felix shows no upper limit to the temperature of the reaction, and that determining the optimum temperature is a matter of "routine experimentation", the Hedges court found that the plain reading of Felix is contrary to the PTO position. See In re Rosenberger, 386 F.2d 1015, 1018, 156 USPQ 24, 26 (CCPA 1967), "[t]his appears to be an extremely strained interpretation of the reference which could be made only by hindsight." Agreeing with Hedges that the prior art as a whole must be considered, the CAFC held that the reference teachings are to be viewed as they would have been viewed by one of ordinary skill. Kimberly-Clark v. Johnson & Johnson, 745 F.2d 1437, 1454, 223 USPQ 603, 614 (Fed. Cir. 1984); In re

Mercier, 515 F.2d 1161, 1165, 185 USPQ 774, 778 (CCPA 1975). "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art". In re Wesslau, 353 F.2d at 241, 147 USPQ at 393.

Similarly to In re Hedges, the present claims on appeal have only been rejected under §103(a) based solely on the Baroody et al. reference. The Examiner alleged that the Baroody et al. reference recognizes pH, viscosity and gelling agents as result-effective variables for the stability of the topical compositions, and that the present claims at most optimized these variables. According to the Examiner, this is not beyond the skill of an ordinary person.

However, as discussed above, the Baroody et al. reference expressly and repeatedly teaches that it is preferable to have a relatively lower viscosity in the benzoyl peroxide suspension and a relatively high viscosity in the final composition when preparing the intended storage stable topical composition. This teaching is to be viewed as it would have been viewed by a person of ordinary skill in the art, as required by In re Hedges. In this regard, the teachings of the Baroody et al. reference should be viewed in their totality, especially those portions that teach away from the presently claimed process where the viscosities are employed in exactly the opposite way,

In addition, the presently claimed process proceeds contrary to the teachings in the Baroody et al. reference. From the teachings in the Baroody et al. reference, it can be said that it is the generally accepted knowledge in the art that combining a benzoyl peroxide dispersion having a relatively lower viscosity with a solution of clindamycin having a relatively higher viscosity is preferable in that it provides for the easy mixing of

the two components to prepare a topical composition comprising benzoyl peroxide and clindamycin. However, the presently claimed process requires the exact opposite of this accepted knowledge in the art by employing the viscosities exactly opposite to the art. Accordingly, this should be considered as evidence of nonobviousness of the present claims 26-31, as required by In re Hedges.

Accordingly, appellants respectfully assert that the Examiner's rejection of the present claims 26-31 is improper. A reversal of the rejection is therefore requested.

E. Unexpected Results and Advantages of the Presently Claimed Process

Appellants additionally assert that the presently claimed process has unexpected results and advantages as compared to the process disclosed in the Baroody et al. reference, and that this rebuts any alleged *prima facie* case of obviousness.

Rebuttal evidence may include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. In re Dillon, 919 F.2d at 692-93, 16 USPQ2d at 1901. Further, rebuttal evidence and arguments can be presented in the specification, In re Soni, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), by counsel, In re Chu, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995), or by way of an affidavit or declaration under 37 CFR 1.132, e.g., Soni, 54 F.3d at 750, 34 USPQ2d at 1687; In re Piasecki, 745 F.2d 1468, 1474, 223 USPQ 785, 789-90 (Fed. Cir. 1984).

The Baroody et al. reference presents, as a benefit or effect of the process disclosed therein, the facilitation of mixing the two components by selecting a gelling agent to have a lower viscosity in the benzoyl peroxide suspension and a higher viscosity

in the final composition. Baroody et al. further presents the storage stability of the topical composition prepared according to this procedure for at least one month, for two months, and for three months or longer. See, Baroody et al. col. 5, lines 51-57 and col. 7, lines 25-30. Further, the combining of the benzoyl peroxide suspension and the clindamycin solution in the Baroody et al. reference is presented to be done prior to use by a pharmacist. See, id. col. 3, lines 26-36.

i. Facilitation of mix, Less degradates and Greater degree of uniformity

In the presently claimed process, the benzoyl peroxide intermediate dispersion has a viscosity of about 60,000 cp to about 250,000 cp and the final composition has a viscosity of about 50,000 cp to about 200,000 cp, wherein the viscosity of the final composition is lower than the viscosity of the benzoyl peroxide dispersion. As discussed above, these viscosities are contrary to the teachings in the Baroody et al. reference and thus are not expected to provide the same beneficial effect as presented in the Baroody et al. reference, because the Baroody et al. reference teaches that "the lower viscosity" of the benzoyl peroxide component makes the combination and mixing with the clindamycin component easier. See, id. at col. 5, lines 53-55. In other words, the expected or predictable effect from using viscosities opposite to those disclosed by Baroody et al., as claimed in the present claims, is that it would make the mixing harder, resulting in worse homogeneity of the final composition.

Unexpectedly, however, it has been found that the presently claimed process, where the final viscosity is lower than the viscosity of the benzoyl peroxide intermediate dispersion, provides compositions that are easier to mix together, contain less degradates, and have a greater degree of uniformity than those compositions previously

known in the art, including the Baroody et al. composition. See, page 15, lines 4-9, of the present application.

ii. Storage stability of the composition prepared

The Baroody et al. reference generally discloses in the specification that the topical compositions remain stable for several months after admixture, see, at col. 3, line 12, and that they may be stored at room temperature and will remain stable, i.e., without substantial loss of efficacy or unacceptable loss of the clindamycin content, for extended periods, typically for at least one month, frequently for two months, and usually for three months or longer, see, at col. 7, lines 25-30. However, Baroody et al. only specifically presents experimental data in this regard in Table 8 of Example 17. In the Example 17, Baroody et al. describes that after two (2) months storage at room temperature, 90% of the original concentration of clindamycin (1.20% to 1.08%) and 99% of the original concentration of benzoyl peroxide (5.87% to 5.83%) remained in the admixed gel. Accordingly, only relying on the experimental data, the composition in the Baroody et al. reference is considered as remaining stable for two months with 90% of the original clindamycin and 99% of the original benzoyl oxide.

Unexpectedly, however, the topical composition prepared according to the presently claimed process has the same amount of clindamycin, i.e., 1.2% of clindamycin, and has a minimum projected stability from seven months to fourteen months at room temperature while maintaining effectiveness. See, page 33, lines 16-19 and the data at page 34. Further, from the Tables 3 and 4 in Example 4 of the present application, it is confirmed that, at 25°C, after three months, the original concentration of clindamycin in the present topical composition remains over 90% (1.24% to 1.13%) and

after six months, the original concentration of benzoyl peroxide remains over 99% (i.e., 5.09% to 5.06%). Accordingly, the topical composition prepared according to the presently claimed process has an improved storage stability in comparison to the topical composition in the Baroody et al. reference. These unexpected results provide direct evidence regarding the non-obviousness of the present claims in view of the Baroody et al. reference.

iii. No Compounding at the time of dispensing

The improved stability provided by the compositions prepared according to the presently claimed processes provides pharmacists and other dispensers of medication with a product which no longer requires compounding at the time of dispensing. Because compounding is no longer required, homogeneity is controlled at the point of manufacture, which improves dosing and ultimately compliance. See, page 33, lines 4-12 of the present application.

The Baroody et al. reference, however, does not present these beneficial properties shown in the topical compositions prepared by the presently claimed process. Actually, in the Baroody et al. reference, the compounding or admixture of the two components is done "prior to use" by a pharmacist, and thus, the benzoyl peroxide suspension and the clindamycin solution are maintained as separate components in a kit before the compounding by the pharmacist. See, id. col. 2, lines 64-65 and col. 3, lines 21-22

As such, appellants assert that the presently claimed process has unexpected improved properties or properties not presented in the Baroody et al. reference, as required by In re Dillon. Also, the supporting evidence and arguments

can be found in the present specification and the Baroody et al. reference themselves, as required by In re Soni.

Accordingly, appellants respectfully submit that any alleged *prima facie* case for obviousness has been rebutted by the unexpected results of the present claims.

CONCLUSION

For the foregoing reasons, appellants respectfully submit that the Examiner's rejection of the presently pending claims 26-31 was erroneous. Accordingly, appellants respectfully request reversal of the Examiner's decision.

The Commissioner is authorized to charge Deposit Account No. 14-0112 for any additional charges in connection with this appeal.

The Examiner is welcomed to contact the undersigned attorney if such contact would be helpful in the further prosecution of this case.

Respectfully Submitted,

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Appendix A

Claims on Appeal

1 - 25. (Cancelled)

26. (Previously presented) A process for preparing a storage-stable topical composition for treating a skin disorder or condition, which comprises the steps of:

a) forming at a temperature of about 15 to about 25 ^{o}C a benzoyl peroxide intermediate dispersion having a viscosity of about 60,000 to about 250,000 centipoises sufficient to yield a composition which contains between about 2.25% and about 12.5% by weight benzoyl peroxide in the final product;

b) forming at a temperature of about 15 to about 25 ^{o}C a clindamycin intermediate solution sufficient to yield a composition which contains between about 0.5% and about 1.5% by weight clindamycin active in the final product; and

c) mixing said benzoyl peroxide intermediate dispersion and said clindamycin intermediate solution under conditions sufficient to yield a benzoyl peroxide and clindamycin mixture having final pH of between about 4.5 to about 5.0,

wherein said mixture has a viscosity lower than the viscosity of the benzoyl peroxide intermediate dispersion, wherein the viscosity of the mixture is of about 50,000 to about 200,000 centipoises, and wherein said composition comprises sufficient inactive ingredients to provide storage stability and effectiveness for a treatment period.

27. (Original) The process of claim 26, wherein said process results in a composition having benzoyl peroxide impurities of not more than about 0.01% by weight.

28. (Original) The process of claim 26, wherein said process results in a composition having clindamycin degradates of not more than about 0.02% by weight.

29. (Original) The process of claim 26, wherein said process results in a composition having benzoyl peroxide impurities of not more than about 0.01% by weight and clindamycin degradates of not more than about 0.02% by weight.

30. (Original) The process of claim 26, wherein said mixture has a final pH of between about 4.6 to about 4.8.

31. (Original) The process of claim 26, wherein said composition has less water by weight as compared to a topical formulation having one of benzoyl peroxide or clindamycin but not both.

32 – 37. (Cancelled)